Claims

1. A method for manipulating a moiety in a microfluidic application, which method comprises:

a) coupling a moiety to be manipulated onto surface of a binding partner of said moiety to form a moiety-binding partner complex; and

b) manipulating said moiety-binding partner complex with a physical force in a chip format, wherein said manipulation is effected through a combination of a structure that is external to said chip and a structure that is built-in in said chip,

thereby said moiety is manipulated.

2. The method of claim 1, wherein the moiety to be manipulated is selected from the group consisting of a cell, a cellular organelle, a virus, a molecule and an aggregate or complex thereof.

3. The method of claim 2, wherein the cell is selected from the group consisting of an animal cell, a plant cell, a fungus cell, a bacterium cell and a recombinant cell.

4. The method of claim 2, wherein the cellular organelle is selected from the group consisting of a nuclei, a mitochondrion, a chloroplast, a ribosome, an ER, a Golgi apparatus, a lysosome, a proteasome, a secretory vesicle, a vacuole and a microsome.

5. The method of claim 2, wherein the molecule is selected from the group consisting of an inorganic molecule, an organic molecule and a complex thereof.

6. The method of claim 5, wherein the inorganic molecule is an ion selected from the group consisting of a sodium, a potassium, a magnesium, a calcium, a chlorine, an iron, a copper, a zinc, a manganese, a cobalt, an iodine, a molybdenum, a vanadium, a nickel, a chromium, a fluorine, a silicon, a tin, a boron and an arsenic ion.

7. The method of claim 5, wherein the organic molecule is selected from the group consisting of an amino acid, a peptide, a protein, a nucleoside, a nucleotide, an oligonucleotide, a nucleic acid, a vitamin, a monosaccharide, an oligosaccharide, a carbohydrate, a lipid and a complex thereof.

8. The method of claim 1, wherein the binding partner is selected from the group consisting of a cell, a cellular organelle, a virus, a microparticle, an aggregate or complex of molecules and an aggregate or complex thereof.

9. The method of claim 8, wherein the cell is selected from the group consisting of an animal cell, a plant cell, a fungus cell, a bacterium cell and a recombinant cell.

10. The method of claim 8, wherein the cellular organelle is selected from the group consisting of a nuclei, a mitochondria, a chloroplast, a ribosome, an ER, a Golgi apparatus, a lysosome, a proteasome, a secretory vesicle, a vacuole and a microsome.

11. The method of claim 8, wherein the dimension of the microparticle is from about 0.01 micron to about several thousand microns.

12. The method of claim 8, wherein the microparticle is selected from the group consisting of a plastic particle, a polystyrene microbead, a glass bead, a magnetic bead, a hollow glass sphere, a metal particle, a particle of complex composition, and a microfabricated free-standing microstructure.

13. The method of claim 1, wherein the moiety is coupled to the surface of the binding partner directly or via a linker.

14. The method of claim 13, wherein the linker is a cleavable linker.

15. The method of claim 1, wherein the moiety is coupled to the surface of the binding partner via a covalent or a non-covalent linkage.

16. The method of claim 15, wherein the linkage between the moiety and the surface of the binding partner is effected via a specific or a non-specific binding.

17. The method of claim 15, wherein the linkage between the moiety and the surface of the binding partner is a cleavable linkage.

18. The method of claim 17, wherein the linkage is cleavable by a chemical, physical or an enzymatic treatment.

19. The method of claim 1, wherein the physical force is selected from the group consisting of a dielectrophoresis, a traveling-wave dielectrophoresis, a magnetic, an acoustic, an electrostatic, a mechanical, an optical radiation force and a thermal convection force.

20. The method of claim 19, wherein the dielectrophoresis force or the traveling wave dielectrophoresis is effected via electrical fields produced by electrodes.

21. The method of claim 19, wherein the magnetic force is effected via a magnetic field produced by a ferromagnetic material.

22. The method of claim 19, wherein the magnetic force is effected via a magnetic field produced by a microelectromagenetic unit.

23. The method of claim 19, wherein the acoustic force is effected via a standing-wave acoustic field or a traveling-wave acoustic field.

24. The method of claim 19, wherein the acoustic force is effected via an acoustic field produced by piezoelectric material.

25. The method of claim 19, wherein the electrostatic force is effected via a direct current (DC) electric field.

26. The method of claim 19, wherein the mechanical force is a fluidic flow force.

27. The method of claim 19, wherein the optical radiation force is effected via a laser tweezers.

28. The method of claim 1, wherein the chip is selected from the group consisting of a silicon dioxide, a silicon nitride, a plastic, a glass, a ceramic, a photoresist and a rubber chip.

29. The method of claim 1, wherein the structure that is external to the chip is an energy source to generate a physical force selected from the group consisting of a dielectrophoresis force, a traveling-wave dielectrophoresis force, a magnetic force, an acoustic force, an electrostatic force, a mechanical force and an optical radiation force.

30. The method of claim 1, wherein the structure that is built-in in the chip comprises a plurality of microunits, each unit, when energized and in combination with the external structure, being capable of effecting the physical force on the binding partner, and further comprising means for selectively energizing any one of the plurality of units.

31. The method of claim 1, wherein the structure that is built-in in the chip comprises a single unit, that, when energized and in combination with the external structure, is capable of effecting the physical force on the binding partner.

32. The method of claim 1, wherein the manipulation is selected from the group consisting of transportation, focusing, enrichment, concentration, aggregation,

trapping, repulsion, levitation, separation, fractionation, isolation and linear or other directed motion of the moiety.

33. The method of claim 1, further comprising a step of decoupling the moiety from the surface of the binding partner after the moiety is manipulated.

34. The method of claim 1, wherein the moiety is a DNA, the binding partner is a porous bead and the DNA is reversibly absorbed onto the surface of the porous bead in a buffer containing high salt concentration.

35. The method of claim 1, wherein the moiety is a DNA and the DNA specifically binds to the surface of a binding partner via sequence specific hybridization or binding to an anti-DNA antibody.

36. The method of claim 1, wherein the moiety is a mRNA and the mRNA specifically binds to the surface of a binding partner that is modified to contain oligo-dT polynucleotide.

37. The method of claim 1, wherein the moiety is a protein and the protein non-specifically binds to the surface of a binding partner that is modified with a detergent.

38. The method of claim 37, wherein the detergent is SDS.

39. The method of claim 1, wherein the moiety is a protein and the protein specifically binds to the surface of a binding partner that is modified with an antibody that specifically recognizes the protein.

40. The method of claim 1, wherein the moiety is not directly manipulatable by a dielectrophoresis force.

41. The method of claim 1, wherein the moiety is not directly manipulatable by a traveling-wave dielectrophoresis force.

42. The method of claim 1, wherein the moiety is not directly manipulatable by a magnetic force.

43. The method of claim 1, wherein the moiety is not directly manipulatable by an acoustic force.

44. The method of claim 1, wherein the moiety is not directly manipulatable by an electrostatic force.

45. The method of claim 1, wherein the moiety is not directly manipulatable by an optical radiation force.

46. The method of claim 1, wherein the moiety to be manipulated is substantially coupled onto surface of the binding partner.

47. The method of claim 1, wherein the moiety to be manipulated is completely coupled onto surface of the binding partner.

48. The method of claim 1, wherein the physical force is not a magnetic force.

49. The method of claim 1, wherein the physical force is selected from the group consisting of a dielectrophoresis, a traveling-wave dielectrophoresis, an acoustic, an electrostatic, a mechanical, an optical radiation and a thermal convection force.

50. The method of claim 1, wherein a plurality of moieties is manipulated.

51. The method of claim 50, wherein the plurality of moieties is manipulated via a plurality of corresponding binding partners.

52. The method of claim 50, wherein the plurality of moieties is manipulated sequentially or simultaneously.

53. A method for isolating an intracellular moiety from a target cell, which method comprises:

a) coupling a target cell to be isolated from a biosample onto surface of a first binding partner of said target cell to form a target cell-binding partner complex;

b) isolating said target cell-binding partner complex with a physical force in a chip format, wherein said isolation is effected through a combination of a structure that is external to said chip and a structure that is built-in in said chip,

c) obtaining an intracellular moiety from said isolated target cell;

d) coupling said obtained intracellular moiety onto surface of a second binding partner of said intracellular moiety to form an intracellular moiety-binding partner complex; and

e) isolating said intracellular moiety-binding partner complex with a physical force in a chip format, wherein said isolation is effected through a combination of a structure that is external to said chip and a structure that is built-in in said chip.

54. The method of claim 53, wherein the biosample is a body fluid.

55. The method of claim 53, further comprising a step of decoupling the first binding partner from the target cell-binding partner complex before obtaining the intracellular moiety from the isolated target cell.

56. The method of claim 53, further comprising a step of transporting the obtained intracellular moiety to a new location for coupling the obtained intracellular moiety onto surface of a second binding partner.

57. The method of claim 53, further comprising a step of transporting the intracellular moiety-binding partner complex to a new location for isolating the intracellular moiety-binding partner complex.

58. The method of claim 53, further comprising a step of detecting the isolated intracellular moiety-binding partner complex.

59. The method of claim 58, further comprising a step of transporting the isolated intracellular moiety-binding partner complex to a new location for detecting the intracellular moiety-binding partner complex.

60. The method of claim 53, further comprising a step of decoupling the intracellular moiety from the isolated intracellular moiety-binding partner complex and detecting the decoupled intracellular moiety.

61. The method of claim 60, further comprising a step of transporting the decoupled intracellular moiety to a new location for detecting the intracellular moiety.

62. A method for generating a cDNA library in a microfluidic application, which method comprises:

a) coupling a target cell to be isolated onto surface of a first binding partner of said target cell to form a target cell-binding partner complex;

b) isolating said target cell-binding partner complex with a physical force in a chip format, wherein said isolation is effected through a combination of a structure that is external to said chip and a structure that is built-in in said chip,

c) lysing said isolated target cell;

d) decoupling and removing said first binding partner from said lysed target cell;

e) coupling mRNA to be isolated from said lysed target cell onto surface of a second binding partner of said mRNA to form a mRNA-binding partner complex;

f) isolating said mRNA-binding partner complex with a physical force in a chip format, wherein said isolation is effected through a combination of a structure that is external to said chip and a structure that is built-in in said chip, and

g) transporting said isolated mRNA-binding partner complex to a different chamber and reverse transcribing said transported mRNA into a cDNA library.

63. The method of claim 62, wherein the target cell is a target blood cell.

64. A method for determining gene expression in a target cell in a microfluidic application, which method comprises:

a) coupling a target cell to be isolated onto surface of a first binding partner of said target cell to form a target cell-binding partner complex;

b) isolating said target cell-binding partner complex with a physical force in a chip format, wherein said isolation is effected through a combination of a structure that is external to said chip and a structure that is built-in in said chip,

c) lysing said isolated target cell;

d) decoupling and removing said first binding partner from said lysed target cell;

e) coupling mRNA to be isolated from said lysed target cell onto surface of a second binding partner of said mRNA to form a mRNA-binding partner complex;

f) isolating said mRNA-binding partner complex with a physical force in a chip format, wherein said isolation is effected through a combination of a structure that is external to said chip and a structure that is built-in in said chip, and

g) determining the quantities of the isolated mRNA molecules,

whereby the gene expression in the target cell is determined.

65. The method of claim 64, wherein the quantities of the isolated mRNA molecules is determined through the reverse transcription of the mRNA molecules to cDNA and determining the cDNA quantities through hybridization of complementary DNA molecules on a chip.

66. The method of claim 64, wherein the target cell is a blood cell.

67. The method of claim 64, wherein the target cell is a cell that has been treated with a drug molecule or a candidate drug molecule.

68. A kit for manipulating a moiety in a microfluidic application, which kit comprises:

a) a binding partner onto the surface of which a moiety to be manipulated can be coupled to form a moiety-binding partner complex;

b) means for coupling said moiety onto the surface of said binding partner; and

c) a chip on which said moiety-binding partner complex can be manipulated with a physical force that is effected through a combination of a structure that is external to said chip and a structure that is built-in in said chip.

69. The kit of claim 68, further comprising instruction(s) for coupling the moiety onto the surface of the binding partner and/or manipulating the moiety-binding partner complex on the chip.